

FIG. 1

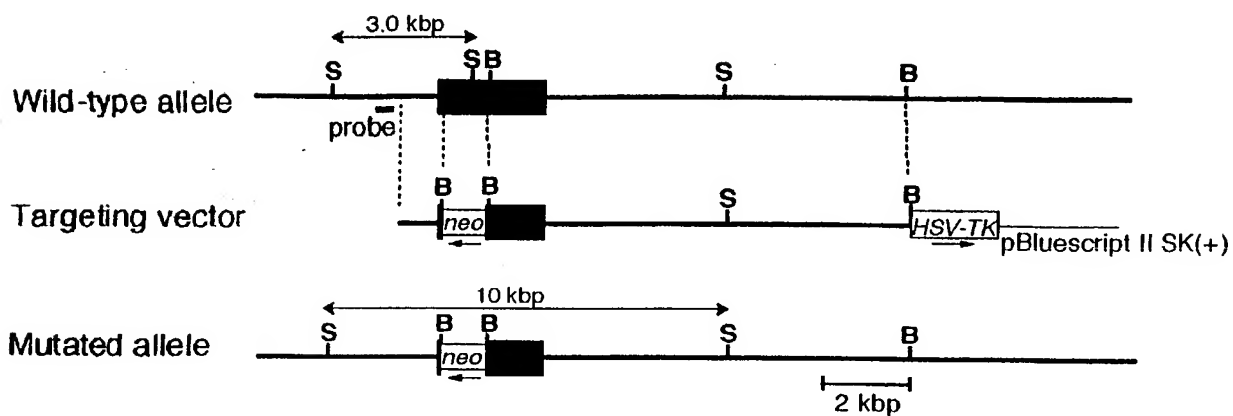


FIG. 2

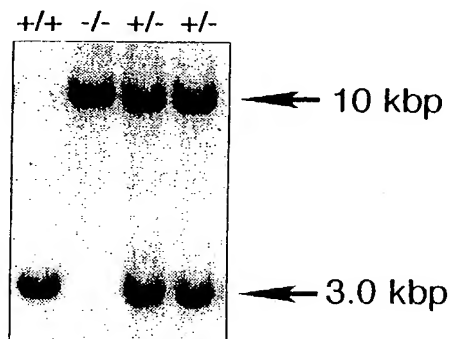
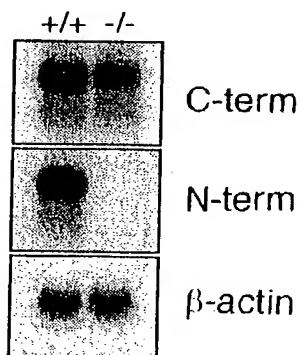


FIG. 3



| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|--|--|--|--|--|--|-----|--|--|--|--|--|--|--|--|--|-----|--|--|--|--|--|--|--|--|--|
| | 87 | | | | | | | | | | 90 | | | | | | | | | | 96 | | | | | | | | | | 100 | | | | | | | | | | 110 | | | | | | | | | |
| + / + : | <u>TCC</u> | <u>AAC</u> | <u>CTG</u> | <u>CGG</u> | <u>CAG</u> | <u>CTG</u> | <u>AAC</u> | <u>CTC</u> | <u>AAG</u> | <u>TGG</u> | <u>AAC</u> | <u>TGT</u> | <u>CCA</u> | <u>CCC</u> | <u>ACT</u> | <u>GGC</u> | <u>CTT</u> | <u>AGC</u> | <u>CCC</u> | <u>TTG</u> | <u>CAC</u> | <u>TTC</u> | <u>TCT</u> | <u>TGC</u> | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | S | N | L | R | Q | L | N | L | K | W | N | C | P | P | T | G | L | S | P | L | H | F | S | C | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| - / - : | <u>S</u> | <u>N</u> | <u>L</u> | <u>R</u> | <u>Q</u> | <u>L</u> | <u>N</u> | <u>L</u> | <u>K</u> | <u>W</u> | <u>I</u> | <u>L</u> | <u>S</u> | <u>T</u> | <u>C</u> | <u>P</u> | <u>R</u> | <u>R</u> | <u>I</u> | <u>R</u> | <u>T</u> | <u>N</u> | <u>D</u> | <u>P</u> | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | TCC | AAC | CTG | CGG | CAG | CTG | AAC | CTC | AAG | TGG | ATT | TTG | TCC | ACC | TGT | CCT | CGA | CGG | ATC | CGA | ACA | AAC | GAC | CCA | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | 87 | | | 90 | | | | | | 96 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

| | | | | | | | | | | | | | | | | | | | | | | | | |
|---------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | 120 | | | | | | | | | | 130 | | | | | | | | | | | | | |
| + / + : | <u>CAC</u> | <u>ATG</u> | <u>ACC</u> | <u>ATT</u> | <u>GAG</u> | <u>CCC</u> | <u>AGA</u> | <u>ACC</u> | <u>TTC</u> | <u>CTG</u> | <u>GCT</u> | <u>ATG</u> | <u>CGT</u> | <u>ACA</u> | <u>CTG</u> | <u>GAG</u> | <u>GAG</u> | <u>CTG</u> | <u>AAC</u> | <u>CTG</u> | <u>AGC</u> | <u>TAT</u> | <u>AAT</u> | <u>GGT</u> |
| | H | M | T | I | E | P | R | T | F | L | A | M | R | T | L | E | E | L | N | L | S | Y | N | G |
| - / - : | <u>T</u> | <u>P</u> | <u>V</u> | <u>R</u> | <u>F</u> | <u>I</u> | <u>L</u> | <u>S</u> | <u>F</u> | <u>Y</u> | <u>C</u> | <u>R</u> | <u>S</u> | <u>P</u> | <u>Q</u> | <u>K</u> | <u>N</u> | <u>S</u> | <u>S</u> | <u>R</u> | <u>R</u> | <u>R</u> | <u>*</u> | |
| | ACA | CCC | GTG | CGT | TTT | ATT | CTG | TCT | TTT | TAT | TGC | CGA | TCC | CCT | CAG | AAG | AAC | TCG | TCA | AGA | AGG | CGA | TAG | |

Figure 2: Cytokine production in wild-type and TLR9^{-/-} mice.

Top Row: Cytokine production in response to CpG ODN.

| Cytokine | Concentration | Condition | Wild-type (ng ml ⁻¹) | TLR9 ^{-/-} (ng ml ⁻¹) |
|-----------|---------------|-----------|----------------------------------|--|
| TNFα | medium | 0.1 | N.D. | N.D. |
| | | 1 | N.D. | N.D. |
| | IFNγ | 0.1 | N.D. | N.D. |
| | | 0.1+IFNγ | ~0.3 | N.D. |
| | | 1 | ~0.5 | N.D. |
| | | 1+IFNγ | ~1.1 | N.D. |
| IL-6 | medium | 0.1 | N.D. | N.D. |
| | | 1 | N.D. | N.D. |
| | IFNγ | 0.1 | ~0.8 | N.D. |
| | | 0.1+IFNγ | ~1.5 | N.D. |
| | | 1 | ~1.6 | N.D. |
| | | 1+IFNγ | ~2.7 | N.D. |
| IL-12 p40 | medium | 0.1 | N.D. | N.D. |
| | | 1 | N.D. | N.D. |
| | IFNγ | 0.1 | ~0.7 | N.D. |
| | | 0.1+IFNγ | ~0.9 | N.D. |
| | | 1 | ~0.5 | N.D. |
| | | 1+IFNγ | ~1.0 | N.D. |

Bottom Row: TNFα production in response to PGN or LPS.

| Stimulus | Concentration | Condition | Wild-type (ng ml ⁻¹) | TLR9 ^{-/-} (ng ml ⁻¹) |
|----------|---------------|-----------|----------------------------------|--|
| medium | 10 | 0.1 | N.D. | N.D. |
| | 1 | N.D. | N.D. | |
| IFNγ | 10 | 0.1 | N.D. | N.D. |
| | 1 | N.D. | N.D. | |
| PGN | 10 | 0.1 | ~1.8 | ~2.5 |
| | 1 | 0.1 | ~1.8 | ~1.8 |
| LPS | 1 | 0.1 | ~1.8 | ~1.8 |
| | 1 | 0.1 | ~2.8 | ~2.8 |

Legend: Black bars = Wild-type; White bars = TLR9^{-/-}. Error bars represent standard deviation. N.D. = Not Detected.

FIG. 6

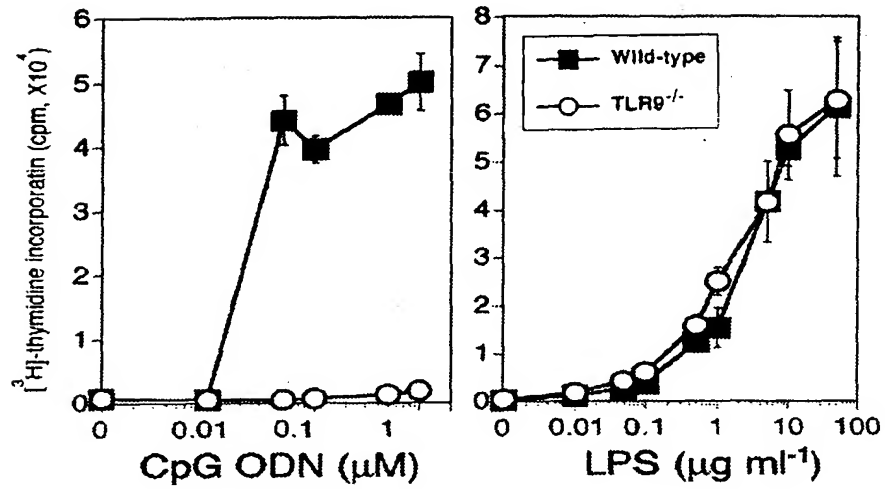


FIG. 7

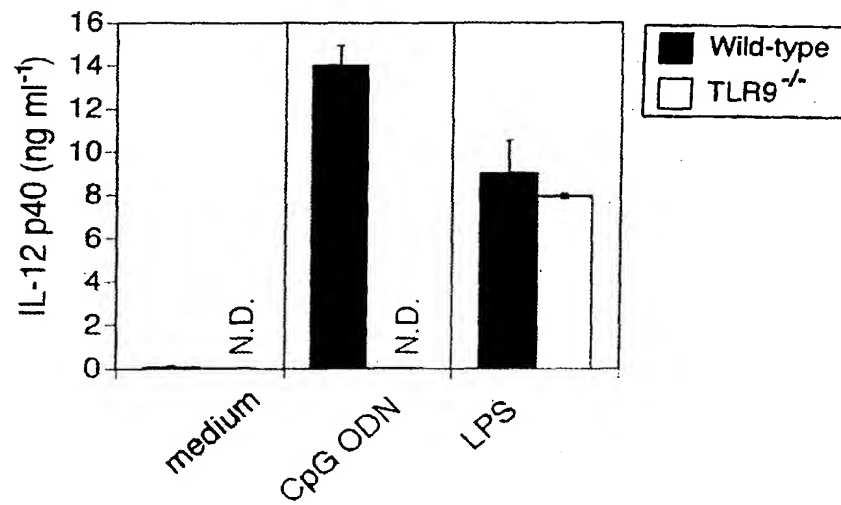


FIG. 8

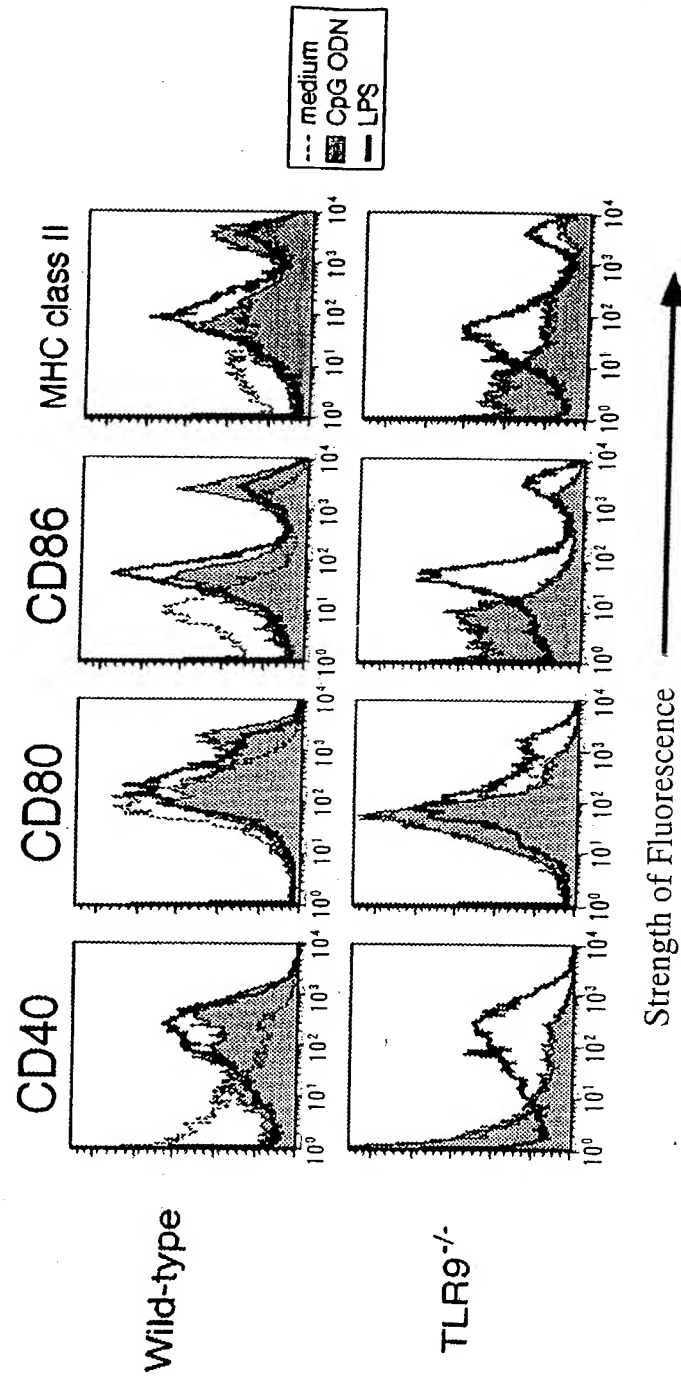


FIG. 9

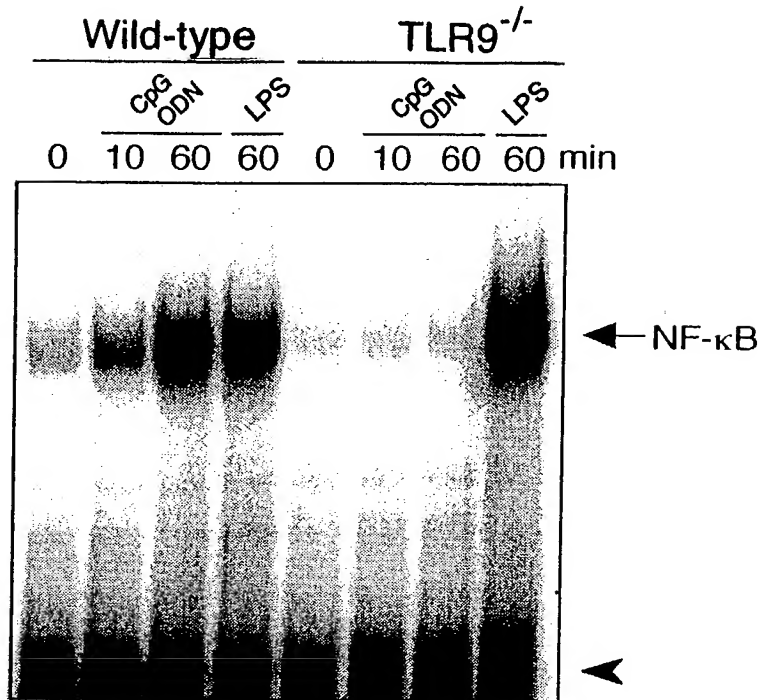


FIG. 10

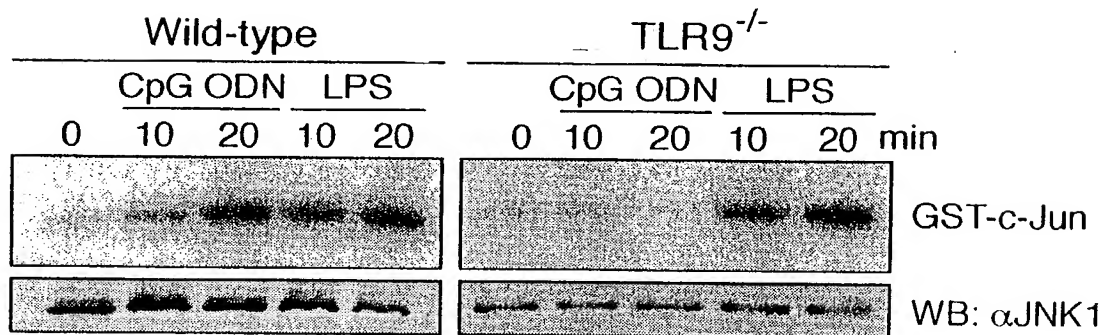


FIG. 11

